Remarks

Claims 1-13, 18-21 and 23-42 are pending in the present Application. Claim 13 has been amended. Support for the amendments can be found at least on page 36, lines 10-13 of the specification as originally filed, and on page 4, lines 8-16 of the specification as originally filed. Claims 13, 18-21 and 23-24 are presently under examination. The remaining claims stand withdrawn as a result of a previous Restriction Requirement. No new matter has been added by any amendment.

Claim rejections under 35 USC § 103

In the Office Action, the PTO rejects Claims 13-14, 18-21 and 23-24 as allegedly obvious under 35 USC § 103(a), in view of the combined teachings of Fisher et al. (US Patent 6,291,469, "Fisher"), Pitts et al. (US Patent 6,489,333, "Pitts") and Trikha et al. (Cancer Research 57: 2522-2528, 1997 "Trikha"). Applicant requests reconsideration and withdrawal of the rejection, because the PTO has not established a *prima facie* case of obviousness for any claim.

In order to establish a *prima facie* case of obviousness of a claim, the PTO must show that a) a cited reference, or combination of references, teaches or suggests each and every claim element; b) there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; and c) there is a reasonable expectation of success. MPEP § 2142.

In the present case, the PTO does not establish that cited references provide a reasonable expectation of success.

In the Office Action, the PTO describes Fisher as teaching spiro compounds that block GPIIb/IIIa fibrinogen receptor (same as $\alpha_{IIb}\beta_3$ receptors), and thereby inhibit platelet aggregation and subsequent thrombus formation.

The PTO describes Pitts as teaching heterocycles that are useful as antagonists of the $\alpha v\beta_3$ and $\alpha_{IIb}\beta_3$ integrins and methods of using the compounds for the inhibition of cell adhesion, treatment of antigenic disorders, inflammation, bone degradation, cancer metastasis, and other conditions mediated by cell adhesion and/or cell migration, and furthermore teaches that tumor

dissemination, or metastasis, involves penetration and transversion of tumor cells through basement membranes and the establishment of self-sustaining tumor foci in diverse organ systems.

The PTO further characterizes Pitts as teaching that development and proliferation of new blood vessels are critical to tumor survival, and that inhibition of angiogenesis in animal models has been shown to result in tumor growth suppression and prevention of metastatic growth. The PTO further characterizes Pitts as setting forth the concepts that an inhibitor which acts against all agonists would represent a more efficacious antiplatelet agent than currently available anti-platelet drugs which are agonist specific, and that platelet glycoprotein IIb/IIIa provides a common pathway for all known agonists, and furthermore teaches compounds that bind to integrin receptors and thereby alter cell-matrix and cell-cell adhesion processes and are useful for inhibition of cell adhesion and treatment of cancer metastases among other indications.

The PTO describes Trikha as teaching that melanoma cells possess "an intracellularly localized pool of high-affinity $\alpha_{IIb}\beta_3$ receptors," and that B16a melanoma cells express the $\alpha_{IIb}\beta_3$ integrin.

The PTO asserts that it would have been *prima facie* obvious to combine Fisher's teachings of spiro compounds which are platelet-specific activated $\alpha_{IIb}\beta_3$ receptor antagonists, Pitt's teachings of use of integrin antagonists for inhibition of cell adhesion and treatment of cancer metastases, and Trikha's teachings of expression of $\alpha_{IIb}\beta_3$ receptors in melanoma cells to reach the presently claimed methods, that the solutions to the prior art problems provide a motivation to combine the references, and that a skilled artisan would be imbued with a reasonable expectation of success.

The PTO has failed to establish *prima facie* obviousness for Claim 13 as currently amended, and claims dependent thereon, at least because the PTO has not shown that the cited references, either singly or in combination, teach all elements of claim 13 as currently amended. In particular, the PTO has not shown that references Fisher, Pitts and Trikha, either singly or in combination, teach administering to a subject an activated $\alpha_{IIb}\beta_3$ receptor antagonist in an amount effective to inhibit the ability of a bone microenvironment to support metastatic migration of a tumor cell within the microenvironment.

In addition, the PTO has not shown that Fisher, Pitts and Trikha, either singly or in combination, provide a reasonable expectation of success. As set forth in the specification, for example on page 36, lines 10-13, the presently claimed methods derive at least in part from the inventors' discovery that inhibition of metastasis into bone through inhibition of $\alpha_{IIb}\beta_3$ receptors can be effected by altering the microenvironment. The Applicant has demonstrated that interfering with $\alpha_{IIb}\beta_3$ receptor activity in a tumor cell's environment can hinder the tumor cell's ability to migrate, regardless of the complement of receptors on the tumor cells themselves. However, the PTO points to no teaching in any of Fisher, Pitts or Trikha that provides a likelihood that tumor cell metastatic migration can be diminished by inhibiting $\alpha_{IIb}\beta_3$ receptor activity in the tumor cell's microenvironment.

Furthermore, even if, *arguendo*, the presence of $\alpha_{IIb}\beta_3$ receptors on the surface of melanoma cells is deemed relevant by PTO, the PTO nevertheless has failed to demonstrate where any of the cited references teach that $\alpha_{IIb}\beta_3$ receptors are present on the surface of melanoma cells. Trikha merely discloses an "**intracellularly localized** pool of high-affinity $\alpha_{IIb}\beta_3$ receptors," which is not a disclosure of the presence of $\alpha_{IIb}\beta_3$ receptors on the cell **surface**.

The PTO thus has not shown that the cited references, either individually or in combination, teach all elements of the claims under examination or provide a reasonable expectation of success, and therefore has not established a *prima facie* case of obviousness for any claim. Applicant, accordingly, requests reconsideration and withdrawal of all claim rejections under 35 USC § 103.

Conclusion

As it is believed the application is in a condition for allowance, Applicant requests prompt and favorable action. All amendments, withdrawals and cancellations are made without prejudice or waiver.

If the PTO deems the claims not to be in condition for allowance, Applicant requests an Advisory Action, and furthermore requests that the Examiner contact the undersigned attorney.

Because the Final Office Action has a mailing date of March 16, 2009, and May 16, 2009 falls on a Saturday, Applicant believes that the filing of this paper on Monday, May 18, 2009 entitles Applicant to receive an Advisory Action. Any communication initiated by this paragraph should be deemed an "Applicant-Initiated Interview."

Applicant believes that there is no fee due at this time. However, if the PTO determines that a payment is due, the Commissioner is hereby authorized to credit any overpayment or to charge any deficiency in connection with this application to Deposit Account 19-3140.

Dated: May 18, 2009

Respectfully submitted,

SONNENSCHEIN NATH & ROSENTHAL LLP

By: /Saul L. Zackson/

Saul L. Zackson, Ph.D.
USPTO Reg. 52,391
SONNENSCHEIN NATH & ROSENTHAL LLP
P.O. Box 061080
Wacker Drive Station, Sears Tower
Chicago, IL 60606-1080
Telephone: 314-259-5817
Fax: 314-259-5959
ATTORNEYS FOR APPLICANT